

AMENDMENTS TO THE CLAIMS

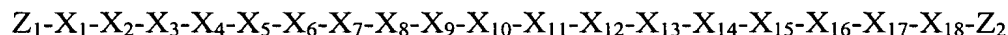
Please cancel claims 1-52.

Please add new claims 53-83 , a shown in the following list of claims:

1.-52. (Canceled).

53. (New) An ApoA-I agonist compound comprising:

(i) a 18 to 22-residue peptide analogue that forms an amphipathic α -helix in the presence of lipids and that comprises formula (I):



or a pharmaceutically acceptable salt thereof, wherein

X_1 is Pro (P), Ala (A), Gly (G), Asn (N), Gln (Q) or D-pro (p);

X_2 is an aliphatic residue;

X_3 is Leu (L);

X_4 is an acidic residue;

X_5 is Leu (L) or Phe (F);

X_6 is Leu (L) or Phe (F);

X_7 is a basic residue;

X_8 is an acidic residue;

X_9 is Leu (L) or Trp (W);

X_{10} is Leu (L) or Trp (W);

X_{11} is an acidic residue or Asn (N);

X_{12} is an acidic residue;

X_{13} is Leu (L), Trp (W) or Phe (F);

X_{14} is a basic residue or Leu (L);

X_{15} is Gln (Q) or Asn (N); X_{16} is a basic residue;

X_{17} is Leu (L);

X_{18} is a basic residue;

Z_1 is H_2N- , or $RC(O)NR-$;

Z_2 is $-C(O)NRR$, $-C(O)OR$ or $-C(O)OH$ or a salt thereof;

each R is independently -H, (C_1-C_6) alkyl, (C_1-C_6) alkenyl, (C_1-C_6) alkynyl, (C_5-C_{20}) aryl, (C_6-C_{26}) alkaryl, 5-20 membered heteroaryl or 6-26 membered alkheteroaryl or a 1 to 4-residue peptide or peptide analogue;

each “ - ” between residues X_1 through X_{18} independently designates an

amide linkage, a substituted amide linkage, an isostere of an amide or an amide mimetic, wherein at least one “-” is a substituted amide linkage, an isostere of an amide or an amide mimetic;

(ii) a 15 to 21-residue peptide analogue according to formula (I) in which at least one and up to eight of residues X_1 , X_2 , X_3 , X_4 , X_5 , X_6 , X_7 , X_8 , X_9 , X_{10} , X_{11} , X_{12} , X_{13} , X_{14} , X_{15} , X_{16} , X_{17} and X_{18} are optionally deleted and wherein at least one “-” is a substituted amide linkage, an isostere of an amide or an amide mimetic; or

(iii) an 18 to 22-residue altered peptide analogue according to formula (I) in which at least one of residues X_1 , X_2 , X_3 , X_4 , X_5 , X_6 , X_7 , X_8 , X_9 , X_{10} , X_{11} , X_{12} , X_{13} , X_{14} , X_{15} , X_{16} , X_{17} and X_{18} is conservatively substituted and wherein at least one “-” is a substituted amide linkage, an isostere of an amide or an amide mimetic; or an N-terminally blocked form, a C-terminally blocked form or an N- and C-terminally blocked form of formula (I).

54. (New) The ApoA-I agonist compound of Claim 53 which exhibits at least about 38% LCAT-activation activity as compared with human ApoA-I.
55. (New) The ApoA-I agonist compound of Claim 54 wherein at least one “-” is a substituted amide linkage.
56. (New) The ApoA-I agonist compound of Claim 55 wherein the substituted amide linkage has the formula $-C(O)NR-$, where R is (C_1-C_6) alkyl, substituted (C_1-C_6) alkyl, (C_1-C_6) alkenyl, substituted (C_1-C_6) alkenyl, (C_1-C_6) alkynyl, substituted (C_1-C_6) alkynyl, (C_5-C_{20}) aryl, substituted (C_5-C_{20}) aryl, (C_6-C_{26}) alkaryl, substituted (C_6-C_{26}) alkaryl, 5-20 membered heteroaryl, substituted 5-20 membered heteroaryl, 6-26 membered alkheteroaryl, or substituted 6-26 membered alkheteroaryl.
57. (New) The ApoA-I agonist compound of Claim 54 wherein the least one “-” is an isostere of an amide.
58. (New) The ApoA-I agonist compound of Claim 57 wherein the isostere of an amide is $-CH_2NH-$, $-CH_2S-$, CH_2CH_2- , $-CH=CH-$ (cis and trans), $-C(O)CH_2-$, $-CH(OH)CH_2-$, or $-CH_2SO-$.

59. (New) The ApoA-I agonist compound of Claim 54 wherein the peptide analogue forms an amphipathic α -helix in the presence of lipids.
60. (New) The ApoA-I agonist compound of Claim 54 wherein the peptide analogue exhibits 40% to 98% helicity in the presence of lipids.
61. (New) The ApoA-I agonist compound of Claim 54 wherein the peptide analogue comprises 40% to 70% hydrophobic residues.
62. (New) The ApoA-I agonist compound of Claim 61 wherein the peptide analogue comprises 50% to 60% hydrophobic residues.
63. (New) The ApoA-I agonist compound of Claim 54 wherein the mean hydrophobic moment, $\langle\mu_H\rangle$, of the peptide analogue is 0.55 to 0.65.
64. (New) The ApoA-I agonist compound of Claim 63 wherein the mean hydrophobic moment, $\langle\mu_H\rangle$, of the peptide analogue is 0.58 to 0.62.
65. (New) The ApoA-I agonist compound of Claim 54 wherein the mean hydrophobicity, $\langle H_o\rangle$, of the peptide analogue is -0.150 to -0.070.
66. (New) The ApoA-I agonist compound of Claim 65 wherein the mean hydrophobicity, $\langle H_o\rangle$, of the peptide analogue is -0.130 to -0.050.
67. (New) The ApoA-I agonist compound of Claim 54 wherein the mean hydrophobicity of the hydrophobic face, $\langle H_o^{pho}\rangle$, of the peptide analogue is 0.90 to 1.20.
68. (New) The ApoA-I agonist compound of Claim 67 wherein the mean hydrophobicity of the hydrophobic face, $\langle H_o^{pho}\rangle$, of the peptide analogue is 0.95 to 1.10.
69. (New) The ApoA-I agonist compound of Claim 54 wherein the pho angle of the peptide analogue is 120° to 160°.
70. (New) The ApoA-I agonist compound of Claim 69 wherein the pho angle of the peptide analogue is 130° to 150°.

71. (New) The ApoA-I agonist compound of Claim 54 wherein the peptide analogue has 3 to 5 positively charged amino acids.
72. (New) The ApoA-I agonist compound of Claim 54 wherein the peptide analogue has 3 to 5 negatively charged amino acids.
73. (New) The ApoA-I agonist compound of Claim 54 wherein the peptide analogue has a net charge of -1, 0, or +1.
74. (New) An ApoA-I agonist-lipid complex comprising an ApoA-I agonist compound and a lipid, wherein the ApoA-I agonist compound is a peptide analogue according to any one of claims 53-73.
75. (New) A pharmaceutical composition comprising an ApoA-I agonist compound according to any one of claims 53-73 or an ApoA-I agonist-lipid complex according to claim 74, and a pharmaceutically acceptable carrier, excipient or diluent.
76. (New) A method of treating a subject suffering from a disorder associated with dyslipidemia, said method comprising the step of administering to the subject an effective amount of the ApoA-I agonist compound of claim 53.
77. (New) The method of Claim 76 in which the disorder associated with dyslipidemia is hypercholesterolemia.
78. (New) The method of Claim 76 in which the disorder associated with dyslipidemia is cardiovascular disease.
79. (New) The method of Claim 76 in which the disorder associated with dyslipidemia is atherosclerosis.
80. (New) The method of Claim 76 in which the disorder associated with dyslipidemia is restenosis.

81. (New) The method of Claim 76 in which the disorder associated with dyslipidemia is HDL or ApoA-I deficiency.
82. (New) The method of Claim 76 in which the disorder associated with dyslipidemia is hypertriglyceridemia.
83. (New) The method of Claim 76 in which the disorder associated with dyslipidemia is metabolic syndrome.